Applicant: Richard T. SAN et al

Serial No.: 08/236,402 Filed: May 2, 1994

Page : 2 of 38

Attorney - Docket No.: 09744-006001 / DITI 107

## **CLAIMS**:

1. (currently amended) A reagent for preparing a scintigraphic imaging agent comprising a specific binding compound that comprises a peptide of from 4 to 100 amino acids having a molecular weight of less than 10,000 daltons, the compound being covalently linked to a radiolabel complexing moiety having a formula selected from the group consisting of:

wherein

(amino acid)<sup>1</sup> and (amino acid)<sup>2</sup> are each independently any primary  $\alpha$ - or  $\beta$ - amino acid that does not contain a thiol group;

Z is selected from the group consisting of cysteine, homocysteine, isocysteine, penicillamine, 2-mercaptoethylamine and 3-mercaptopropylamine;

 $R^1$  is lower ( $C^1$ – $C^4$ ) alkyl or a covalent linkage to the compound;

wherein wherein, when Z is cysteine, homocysteine, isocysteine or penicillamine, Z comprises a carbonyl group covalently linked to a hydroxyl group, a NR<sup>3</sup>R<sup>4</sup> group wherein R<sup>3</sup> and R<sup>4</sup> are each independently H or lower (C<sup>1</sup>–C<sup>4</sup>) alkyl, an amino acid, or a peptide comprising 2 to 10 amino acids;

and



Applicant: Richard T. LEAN et al.

Serial No.: 08/236,402 Filed: May 2, 1994 Page: 3 of 38 Attorney's Docket No.: 09744-006001 / DITI 107

II.

wherein

Y is selected from the group consisting of cysteine, homocysteine, isocysteine, penicillamine, 2-mercaptoacetate and 3-mercaptopropionate;

(amino acid)<sup>1</sup> and (amino acid)<sup>2</sup> are each independently any primary  $\alpha$ - or  $\beta$ - amino acid that does not contain a thiol group;

R<sup>2</sup> is selected from the group consisting of H, a lower (C<sup>1</sup>-C<sup>4</sup>) alkyl, and a covalent linkage to the compound;

wherein wherein, when Y is cysteine, homocysteine, isocysteine or penicillamine, Y comprises an amino group covalently linked to -H, an amino acid, or a peptide comprising 2 to 10 amino acids; and

wherein wherein, the moiety is linked to the compound through R<sup>1</sup>, R<sup>2</sup>, a sidechain group of (amino acid)<sup>1</sup>, a sidechain group of (amino acid)<sup>2</sup>, an amino group of cysteine, homocysteine, isocysteine or penicillamine, or a carboxyl group of cysteine, homocysteine, isocysteine or penicillamine.

2. (currently amended) The reagent of claim 1 wherein the radiolabel complexing moiety is selected from the group consisting of comprises

and or



Applicant: Richard T. LAN et al.

Serial No.: 08/236,402 Filed: May 2, 1994 Page: 4 of 38 Attorney's Docket No.: 09744-006001 / DITI 107

(mercaptocarboxylic acid) (amino acid)<sup>1</sup> (amino acid)<sup>2</sup>, (mercaptocarboxylic acid) (amino acid)<sup>2</sup> (amino acid)<sup>1</sup>

## wherein

(amino acid)<sup>1</sup> and (amino acid)<sup>2</sup> are each independently any primary  $\alpha$ - or  $\beta$ -amino acid;

(amino thiol) is selected from the group consisting of cysteine, isocysteine, homocysteine, penicillamine, 2-mercaptoethylamine, 2-mercaptoethylamine and 3-mercaptopropylamine; and

(mercaptocarboxylic acid) is selected from the group consisting of cysteine, isocysteine, homocysteine, penicillamine, 2-mercaptoacetic acid, acid and 3-mercaptopropionic acid.

- 3. (currently amended) The reagent of Claim 2 wherein the radiolabel complexing moiety is selected from the group consisting of comprises

  -Gly-Gly-Cys -Gly-Gly-Cys and or Cys-Gly-Gly-.
- 4.-5. (cancelled)
- 6. (currently amended) The reagent of Claim 5 1 wherein the peptide compound and the moiety are linked through one or more amino acids.
- 7. (currently amended) A scintigraphic imaging agent comprising the reagent according to Claim 1 wherein the radiolabel binding complexing moiety is bound to a radiolabel.



Applicant: Richard T. LAN et al.

Serial No.: 08/236,402 Filed: May 2, 1994 Page: 5 of 38 Attorney's Docket No.: 09744-006001 / DITI 107

8. (original) The reagent of Claim 7 wherein the radiolabel is technetium-99m.

9.-10. (cancelled)

11. (original) A complex formed by reacting the reagent of Claim 1 with technetium-99m in the presence of a reducing agent.

- 12. (original) The complex of Claim 11, wherein the reducing agent is selected from the group consisting of a dithionite ion, a stannous ion and a ferrous ion.
- 13. (original) A complex formed by labeling the reagent of Claim 1 with technetium-99m by ligand exchange of a prereduced technetium-99m complex.
- 14. (original) A kit for preparing a radiopharmaceutical preparation, said kit comprising a sealed vial containing a predetermined quantity of the reagent of Claim 1 and a sufficient amount of reducing agent to label the reagent with technetium-99m.
- 15. (original) A method for labeling a reagent according to Claim 1 comprising reacting the reagent with technetium-99m in the presence of a reducing agent.

Applicant: Richard T. DEAN et al.

Serial No.: 08/236,402 Filed: May 2, 1994 Page: 6 of 38 Attorney's Docket No.: 09744-006001 / DITI 107

16. (original) The method of Claim 15, wherein the reducing agent is selected from the group consisting of a dithionite ion, a stannous ion and a ferrous ion.

- 17. (currently amended) A method for imaging a site within a mammalian body comprising administering an effective diagnostic amount of the reagent of Claim 2 8 and detecting a radioactive signal from the technetium-99m localized at the site.
- 18. (cancelled)
- 19. (currently amended) The reagent of Claim 5 1 wherein the peptide comprises a linear peptide or a cyclic peptide.
- 20. (previously amended) The reagent of Claim 1 wherein the compound binds to a thrombus site.
- 21. (previously amended) The reagent of Claim 1 wherein the compound binds to a site of an infection.
- 22-37. (cancelled)
- 38. (new) A method according to Claim 17 wherein radiolabel complexing moiety comprises

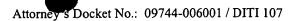
or

(mercaptocarboxylic acid)—(amino acid)<sup>2</sup>—(amino acid)<sup>1</sup>



Applicant: Richard T. DEAN et al.

Serial No. : 08/236,402 Filed : May 2, 1994 Page : 7 of 38



## wherein

(amino acid)<sup>1</sup> and (amino acid)<sup>2</sup> are each independently any primary  $\alpha$ - or  $\beta$ -amino acid;

(amino thiol) is selected from the group consisting of cysteine, isocysteine, homocysteine, penicillamine, 2-mercaptoethylamine and 3-mercaptopropylamine; and

(mercaptocarboxylic acid) is selected from the group consisting of cysteine, isocysteine, homocysteine, penicillamine, 2-mercaptoacetic acid and 3-mercaptopropionic acid.

